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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/934,249	08/21/2001	Richard T. Lee	P0738/7001 (ERP/KA)	6506

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/934,249	LEE ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-11,68,80-83 and 86-90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 8-11, 68, 80-83, 86-90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8-30-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Currently claims 1-4, 8-11, 68, 80-83, and 86-90 are pending and under consideration in the application. Claims 1-4, 8-11, 68, and 80-84, and 86-88 were rejected in the prior action, mailed on July 13, 2004. In the Response filed on January 13, 2004, the Applicant amended claims 1, 3, 4, and 80; and cancelled claim 84; and added claims 89 and 90.

2. Because this action raises a new ground of rejection, the action is made Non-Final.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on August 30, 2004 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Claim Objections

4. **(Prior Objection- Withdrawn)** Claim 84 was objected to under 37 CFR 1.75 as being a substantial duplicate of claim 9. In view of the cancellation of the claim, the objection is withdrawn.

5. **(New Rejection)** Claims 1-4, 8-11, 68, 80-83, 86-90 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The claims are rejected as lacking a substantial and specific utility. In particular, the application has asserted no utility specific to the claimed inventions. There is no identification of a function for the protein encoded by SEQ ID

NO: 1, nor is there any correlation of the presence of the polynucleotide (i.e. gene expression of SEQ ID NO: 1) or the protein with any specific cardiac pathology. Because the application has not provided a specific function for the claimed nucleotides, or identified as specific disorder that the nucleotides may be used to diagnose, the claims are rejected as lacking a substantial and specific utility.

6. **(New Rejection)** Claims 10 and 11 rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims read on host cells transformed or transfected with a claimed expression vector. However, the claims do not require that the host cells are isolated, and therefore read on host cells within a human being. Because the claims read on such host cells, they read on a human being, which is not patentable subject matter. It is suggested that the claims be amended to read on an - - isolated- - host cell.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. **(Prior Rejection- Withdrawn)** Claims 8-11, 84, and 86 were rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. In view of the Applicant's arguments submitted in the Response, the rejection is withdrawn.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. **(Prior Rejection- Withdrawn)** Claims 1-3, 8, 10, 11, 82, and 83 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims currently read on various nucleic acid compositions, providing no requirement as to the function of the nucleic acids. The Applicant's arguments refer to the use of the claimed compositions as diagnostic agents. In view of this, and because the claims no longer refer to apoptotic activity, the rejection is withdrawn as redundant to the enablement rejection below.

11. **(Prior Rejection- Maintained)** Claims 1, 3, 4, 68, 80, 81, 87, and 88 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims were rejected because the application does not enable those in the art to practice the claimed invention as the application does not teach what disorders may be diagnosed using the claimed nucleic acids, or the encoded peptides. The rejection is extended to claims 2, 8-11, 82, 83, 86, and 89-90 because, as the application has neither

demonstrated the anti-apoptotic activity of the encoded polypeptides, or identified what disorders the claimed compositions may be used to diagnose, the application has not enabled those in the art to use any of the claimed compositions, or products derived therefrom. Thus, claims 1-4, 8-11, 68, 80-83, 86-90 are rejected.

The Applicant traverses the rejection on the basis that "the specification has clearly established that MIVR-1is upregulated when mechanically deformed," and that such proteins are useful as targets for detecting cardiac strain of pathologic conditions in vivo. However, while the application demonstrates that MIVR-1 is upregulated in an in vitro model of cell strain, there is no identification or demonstration in the application that the production of MIVR-1 is determinative of a pathologic condition. Rather, cardiac cells are constantly under strain as the heart is continuously beating. See e.g., U.S. 2002/0072674, page 1. Thus, the demonstration that MIVR-1 is produced when a cardiac cells is subjected to strain does not demonstrate the protein is indicative of a pathologic condition. Rather, due to the constant strain on such cells, the protein is likely to be produced by normal cardiac cells.

The application provides no evidence that MIVR-1 is expressed only, or expressed differentially, in cells undergoing a pathologic condition. There is no indication as to what the relative expression levels of MIVR-1 are between healthy and unhealthy cardiac cells. Absent some demonstration that MIVR-1 is in fact an indicator of a pathologic condition, and some indication as to how one of ordinary skill in the art may use the claimed MIVR-1 compositions to determine the presence or absence of a particular pathologic condition, those in the art would not be able to use the claimed inventions absent discovering for themselves the function of the MIVR-1 protein, and/or the association between the protein or its expression with specific

cardiac pathologies. Because the application does no more than indicate that cardiac under strain produces the protein, and provides no demonstration or guidance as to how the protein or the claimed compositions may be used, or what pathologies if any they may be used as indicators for, the application has not enabled those in the art to use the claimed inventions.

For these reasons, and for the reasons of record, the Applicant's amendments are arguments are not found persuasive. The rejection is therefore maintained.

12. **(New Rejection)** Claims 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 10 and 11 are drawn to host cells comprising the claimed nucleic acids or expression vectors. The claims are not drawn to isolated host cells, thus, when given the broadest reasonable interpretation, read on host cells comprised within a living organism such as a transgenic animal or a human gene therapy patient. It is noted that the specification contemplates gene therapy on pages 30-31, and transgenic animals on page 30. The specification is not enabling for host cells comprised within either the human patient or the transgenic animal for the reasons set forth below.

(A) As drawn to gene therapy

The instant specification does not teach how to overcome problems with in vivo delivery and expression with respect to the administration of the claimed nucleic acids or viral vectors comprising said nucleic acids. The state of the art as of the priority date sought for the instant application is that in vivo gene delivery is not well developed and is highly unpredictable. For instance, Verma et al. (Nature, 1997, Vol. 389, pp. 239-242) teaches that the Achilles heel of gene therapy is gene delivery. Verma et al state that the ongoing problem is the inability to deliver genes efficiently and to obtain sustained expression (page 239, column 3). Eck et al (Gene-Based Therapy, In: The Pharmacological Basis of Therapeutics, Goodman and Gilman, Eds., 1996, pp. 77-101) teach that the fate of the DNA vector itself with regard to the volume of distribution, rate of clearance into tissues etc., the in vivo consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA the level of mRNA produced, the stability of the mRNA produced in vivo, the amount and stability of the protein produced and the proteins compartmentalization or secretory fate within the cell are primary considerations regarding effective therapy. Eck et al state that these factors differ dramatically on the vector used, the protein being produced, and the disease being treated (Eck et al bridging pages 81-82).

As of the priority date sought, it was well known in the art how to infect or transfect cells in vitro or ex vivo with viral vectors. However, using viral vectors to deliver DNA to an organism in vivo, or using infected or transfected cells to deliver nucleic acids which encode a particular protein sequence to an organism in vivo is in the realm of gene therapy, and as of the priority date sought, highly unpredictable in view of the complexity of in vivo systems. Orkin et al state ("Report and Recommendation of the Panel to Assess the NIH Investment in Research on Gene Therapy", NIH, 1995) clinical efficacy had not been definitively demonstrated with any gene therapy protocol (page 1, second paragraph). Orkin et al defines gene therapy as the transfer of DNA into recipient cells either ex vivo or in vivo (page 7, under the heading "Gene transfer"), thus encompassing the instant claims drawn to the administration of antigen presenting cells transfected or infected ex vivo. Orkin et al concludes that, "none of the available vector systems is entirely satisfactory, and many f the perceived advantages of vector systems have not been experimentally validated. Until progress is made in thee areas, slow and erratic success in applying gene transfer methods to patients can be expected" Orkin et al comment that direct administration of DNA or DNA in liposomes is not well developed and hindered by the low efficiency of gene transfer (page 8, paragraph 5). Orkin et al teach that adequate expression of the transferred genes is essential for therapy, but that in 1995 current data regarding the level and consistency of expression of transferred genes in animal models was unknown. Orkin et al states that in protocols not involving ex vivo infections/transfection, it is necessary to target the expression of the transferred genes to the appropriate tissue or cell type by means of regulatory sequences in gene transfer vectors. The specification does not teach a vector having a specific regulatory sequence which would direct the expression of the nucleic acids within the appropriate tissue type.

The specification does not remedy any of the deficiencies or the prior art with regard to gene therapy. Given the lack of any guidance from the specification on any of the above issues pointed out by Verma or Eck or Orkin. One of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to practice the methods of claims.

(B) As drawn to a transgenic animal

The specification states on page 30 that genetically engineered host cells can be used to produce transgenic non-human animals. The specification does not provide guidance in the making of a transgenic animal comprising the instant recombinant polynucleotides or transformed cells. In the art of producing transgenic animals, the phenotype of the resultant transgenic animal is not always predicable or viable. The vectors to be used for directing the expression of transgenic in a given tissue or in all tissues must contain the appropriate regulatory regions (Houdebine, Journal of Biotechnology, 1994, Vol. 34, pp. 269-287), see bridging pages 272-273) and expression is heavily dependent on the site of integration in the host genome, and the site of integration is presently unpredictable (Houdebine, page 277, column 1). Therefore, it is concluded that one of skill in the art would undergo undue experimentation in order to make a transgenic animal comprising the claimed host cells.

Amendment of the claims to recite "isolated host cell" would overcome this rejection.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. **(Prior Rejection- Withdrawn)** Claims 1, 4, 68, and 88 were rejected under 35 U.S.C. 102(e) as being anticipated by Zhong et al. (U.S. 20020064771). In view of the amendment of the claims, the rejection is withdrawn.

15. **(Prior Rejection- Withdrawn)** Claims 1, 4, 68, 80, and 88 were rejected under 35 U.S.C. 102(e) as being anticipated by either of Matson et al. (U.S. 5,981,185), or Weiner et al. (U.S. 20030026801).). In view of the amendment of the claims, the rejection is withdrawn.

16. **(New Rejection)** Claims 1, 4, 68, 81, 88, and 89 are rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al., Genomics 66: 257-63 (of record in the January 2003). These claims are drawn to isolated nucleic acids that hybridize to SEQ ID NO: 3, or complements thereof.

Xu teaches a DNA probe of 22 residues that is complementary to nucleotides 426-447 of SEQ ID NO: 3. See page 258 (antisense probe in first (carryover) paragraph in the right column).

The reference also teaches a probe that corresponding to residues 368-387 of SEQ ID NO: 3. Page 258 (sense probe, third full paragraph in right column). The reference therefore anticipates the indicated claims.

Conclusion

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

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